Draft OSWER Interim Risk Methodology for Asbestos

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Objectives of Interim Methodology

- Provide a state of the science approach for quantifying asbestos cancer risk using TEM data.
- Evaluate the potency associated with different classes of asbestiform minerals (amphibole or serpentine).
- Evaluate the potency associated with different fiber dimensions (length and width).

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Overview of Interim OSWER Risk Methodology

- Based on meta-analysis of epidemiology studies;
- Uses the same general risk models as the IRIS assessment;
- Uses surrogate TEM data to examine the influence of particle size on potency;
- Evaluates numerous strategies for stratifying particle sizes.

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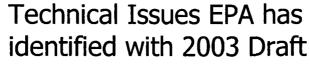# History of the OSWER Interim Risk Methodology

- OSWER has been working on this methodology for a number of years:
  - Initial work began in R9;
  - The Libby response re-ignited the effort;
  - In 2003, we conducted peer consultation on 2001 draft.
- Earlier drafts often called "Berman and Crump Methodology" because these contractors performed the initial work.

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2003 Peer Consultation

- Eleven experts reviewed the draft methodology.
- Strongly endorsed approach:
    - That potential differences in potency associated with mineral type and particle size.
- They also recommended:
    - Increasing transparency and reproducibility;
    - Conducting sensitivity and uncertainty analysis;
    - Considering other bin definitions.

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Technical Issues EPA has identified with 2003 Draft

- Methodology for 2003 draft is based on fitting a set of fitted parameters (study-specific potencies). Current approach fits measured data (cancer deaths).
- Method for specifying uncertainty is semi-arbitrary, complex, not intuitive:
    - Assumes lognormal uncertainty around study-specific potencies
        - $KL[j] \sim LN(\mu, \sigma)$
        - There seems to be little basis for this assumption;
    - Lognormal distributions cannot accept zero or negative values;
    - Method for quantifying uncertainty (the σ term) in the studies is complicated; hard to judge if it achieves appropriate weightings;
    - We think it is better to specify uncertainty in the input data items themselves.

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Need to Advance Methodology

- Parties inside and outside of the Agency have been using, or considering the use, of earlier drafts of this methodology.

- Changes are needed to address technical issues identified by EPA and the concerns of the 2003 peer consultation panel.

- The methodology needs to be peer reviewed before its use can be supported by EPA.

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Follow-up to 2003 Consultation

- Since the peer consultation OSWER has been improving the methodology to:
  - Facilitate reproducibility;
  - Improve transparency.
- OSWER has recently completed sensitivity and uncertainty analyses on 2003 draft.
- OSWER is completing an internal review conducted with representatives from regional and program offices
- Planning a two-stage SAB review: peer consultation on methodology, followed by peer review.
- After peer review, OSWER plans to use this risk methodology for site-specific assessments on an interim basis until the IRIS reassessment is complete.

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Methodology Details

- Based solely on meta-analysis of epidemiology studies;
  - All studies with sufficient exposure-response data are considered;
  - Probabilistic techniques (PDFs) are used to characterize the uncertainty and variability associated with each study.
- Uses the same general models as the Airborne Asbestos Health Assessment Update (USEPA, 1986), which was used to derive the IRIS assessment:
  - Relative risk model for lung cancer;
  - Absolute risk model for mesothelioma.

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Use of Surrogate Data

- None of the available epidemiology studies used TEM to obtain particle size data.
- A set of studies that have employed TEM to characterize fibers in various work environments are used as a surrogate.
- The surrogate data allow us to develop a risk metric based on fiber size and type rather than on PCM fiber counts.

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Multi-Bin Approach

- Influence of fiber dimensions and mineralogy on potency are evaluated using "bins."
    - For example, separate potencies are derived for bins of amphibole and serpentine fibers (see example).
- Evaluating 20 different strategies.

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Example of Binning Approaches

One Bin	Two Bins	Four Bins
All PCM fibers (Amphibole & Chrysotile) All lengths (>= 5 um)	Amphiboles All lengths (>= 5 um)	Short amphiboles (5-10 um)
		Long amphiboles (>10 um)
	Chrysotile All lengths (>= 5 um)	Short chrysotile (5-10 um)
		Long chrysotile (>10 um)

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Binning strategies for 1-bin model

Designation	Mineral Type	Length (um)	Width (um)
1P	Amphibole and chrysotile	>5	>0.25
1A		>0	< 0.4
1B		>5	
1C		>10	
1D		>0	< 1.5
1E		>5	
1F		>10	

Binning Strategies for Two and Four Bins Models

Number of Bins	Designation	Mineral Type	Length (um)	Width (um)
2	2P	Amphibole or Chrysotile	> 5	≥ 0.25
	2A		All	< 0.4
	2B		> 5	< 0.4
	2C		> 10	< 0.4
	2D		All	< 1.5
	2E		> 5	< 1.5
	2F		> 10	< 1.5
4	4A	Amphibole or Chrysotile	0-5 > 5	< 0.4
	4B		5-10 > 10	< 0.4
	4C		0-10 > 10	< 0.4
	4D		0-5 > 5	< 1.5
	4E		5-10 > 10	< 1.5
	4F		0-10 > 10	< 1.5

Note: The seven binning strategies presented for two bin model were also examined for one bin model.

Model Outputs

- Uncertainty distributions for each bin-specific potency factor
- Uncertainty distributions for mixture-specific potency factors
- Risk management or policy decisions could guide the selection of potency estimates from uncertainty distribution (mean and/or upper-bound).

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Example Mixture-Specific Potency Factor Uncertainty Distributions

Y-axis = Cumulative Probability

X-Axis = Mixture –Specific Potency for mesothelioma

10 long: 1 short   3 long: 1 short   Fraction Amphibole

95%

30%

1%

Analysis of Comments from Interagency Review

As number of recommend changes are being made including:

- Corrected errors noted by reviewers
- Clarified purpose/intent of document
- Modified inputs to allow use of different TEM data sets for chrysotile and amphibole particle sizes distributions in mixed exposure locations
- Developed improved statistical procedure for comparison of different binning strategies
- Implemented one-step fitting of study-specific α terms in lung cancer studies

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Next Steps

- Currently responding to internal review comments;
- Planning to meet with NCEA to discuss next steps;
- Draft charge questions with assistance from EPA and other government scientists;
- Science Advisory Board consultation;
- Conduct full interagency review and public comment prior to final peer review;
- Final SAB peer review.

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Questions (part 1):

- When the work will be completed?
  - Expect to complete SAB review in 2008
- How could it support the Libby Risk Assessment?
  - The Interim Methodology will provide a method for assessing risk associated with exposure to all types of asbestos, including amphiboles.
  - Allows (requires) use of TEM data on exposure mixture.
  - Includes consideration of lung cancer data from Libby miner cohort.

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Questions (part 2):

- What are its limitations or uncertainties?
  - Uncertainties associated with exposure are common to epidemiologic evaluations;
  - Application of surrogate particle size data.
- Can studies be done to address its data gaps?
  - New TEM analysis of exposure data from some of the cohorts would provide a method for validating surrogate approach.

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